Using a Mass Selective Chemical Sensor to Help Identify Unknowns

Application

Gas Chromatography

April 1999

Authors

C. Kai Meng
Philip L. Wylie
Agilent Technologies, Inc.
2850 Centerville Road
Wilmington, DE 19808-1610
USA

Abstract

Agilent Technologies has developed a chemical sensor, the Agilent 4440A, which can rapidly distinguish among similar products with volatile constituents. The instrument consists of a modified Agilent headspace autosampler coupled directly to a modified Agilent mass selective detector. Unlike headspace gas chromatography with mass selective detection (HS/GC/MS), this system has no GC, and there is virtually no separation of the volatile constituents. Instead, the headspace volatiles are transferred directly to the mass selective sensor, which typically gives rise to a single broad peak composed of all the volatile constituents in the sample. Because the mass spectra of all these compounds are also overlaid, multivariate analysis and pattern recognition software are used to classify the samples.

The advantages of this system over conventional HS/GC or HS/GC/MS, are its speed and ease of use. Samples can be analyzed every 2 to 6 minutes, depending upon the amount of headspace equilibration time required, and operator training takes less than an hour. This application note discusses how the 4440A chemical sensor has been used to discriminate among various products. Most interestingly, this application note also shows how to use the information from the 4440A chemical sensor to identify one or more "impurities" when out-of-spec samples are found.

Key Words

Chemometrics, chemical sensor, electronic nose, mass spectrometer (MS), mass selective sensor, out-of-spec, discrimination, unknown, headspace, PCA, x-residuals

Introduction

A chemical sensor has been designed to use an Agilent mass selective detector (MSD) instead of more typical solid state sensors. The 4440A chemical sensor consists of a headspace autosampler, a mass selective sensor, and chemometrics/pattern recognition software (Pirouette® from Infometrix® in Woodinville, Washington) for data analysis and model building.

Unlike headspace gas chromatography with mass selective detection (HS/GC/MS), this system has no GC, and there is virtually no separation of the volatile constituents. Instead, the headspace volatiles are transferred directly to the mass selective sensor, which typically gives rise to a single broad peak composed of all the volatile constituents in the sample. Because the mass spectra of all these compounds are also overlaid, multivariate analysis and pattern recognition software are used to classify the samples.

Using Principal Components Analysis (PCA), one of the multivariate analysis routines available in the Pirouette software, the composite spectrum of one sample becomes a dot on a three-dimensional PCA plot. The dots from similar samples cluster together on the plot. Samples that differ in their volatile components1 (because of composition, grade, impurity, manufacturing processes, and so forth) cluster in different locations on the three-dimensional PCA plot. Therefore, it is easy to see sample clusters and outliers by simply rotating the three-dimensional plot on the computer screen. Because the detector measures a highly-reproducible mass fragment pattern, the system can help identify the unknown chemical that causes the change.

The way that the data are used and presented is quite different between the mass selective sensor and GC/MS. In the mass selective sensor using PCA, each m/z is processed independently. In other words, each m/z is treated as an independent signal for the PCA. However, GC/MS typically gives the total ion chromatogram (TIC), which is the sum of all the m/z responses at a particular time. When comparing samples, a small variation at a mass unit, for example 137, does not make any visual difference in the TIC, but it makes a big difference in calculating the principal components. Therefore, it is easy to spot the change on a PCA plot. One might be able to see the difference of m/z 137 by plotting the GC/MS extracted ion chromatograms. However, when variation occurs, one has to know what mass(es)— 137, in this example—to plot in the first place, which is not possible for unknowns.

Pirouette is used to build a model based on a collection of representative samples that are used to "train" the chemical sensor. The samples used to train the sensor should be representative of those one expects to screen in the future. They could represent "good" and "bad," grade A, B, C, country of origin, adulterated and unadulterated, fresh and aged, brand or manufacturer, and so on.

Once the chemical sensor has been trained by a person who is familiar with the various sample types, an operator can use the sensor to classify unknowns or identify out-of-spec materials. When unknown samples are run, their composite mass spectral fingerprints are compared to those of the known samples and a classification or pass/fail decision is made.

Experimental

Samples of any nature are loaded in 10-mL (or 20-mL) vials and then sealed with crimp caps and PTFE-coated silicone rubber septa. A typical sample amount is 5 µL to 5 mL for liquids and 1 to 2 grams for solids. After the vials are loaded in a headspace autosampler and heated (and/or shaken) for a predefined period of time (typically 5 to 30 minutes), 1 mL (or 3 mL) of the headspace from the vial is sent to the mass selective sensor. With the six-sample overlap-heating feature of the headspace autosampler, samples are typically analyzed every 2 to 6 minutes. Therefore, a tray of 44 samples can be analyzed in 2 to 5 hours.

The Agilent chemical sensor is designed to operate over a wide user-selectable mass range of 2 to 800 amu. However, for volatile components, a mass range of about 35 to 180 amu is typically used for samples heated up to 100 °C. This commonly used mass range eliminates any effects from water or air on data integrity. Without any separation, 1–3 mL of the headspace from the vial rushes through the MS in tens of seconds. Several scans from m/z 35 to 180 are recorded every second. The final spectrum is a composite of a hundred or mo re scans. Because only volatile samples are introduced, the mass sensor's source rarely, if ever, needs cleaning.

Typical headspace autosampler and mass sensor operating parameters are listed in table 1.

Table 1. Typical Experimental Parameters for the 4440A Chemical Sensor

Headspace Autosampler		Mass Selective Sensor	
Oven	65–110 °C	Data acquisition mode	Scan
Loop	65–125 °C	Scan range	35–180 amu
Transfer line	75–135 °C	Threshold	150
Interface	85–145 °C	Solvent delay	0.45 min
		End time	0.85 min
Sample loop	1 mL or 3 mL		
HS cycle time	2–6 min		
Vial equilibration time	5–30 min		
Pressurize time	0.30 min		
Loop fill time	0.15 min		
Loop equilibration time	0.02 min		
Inject time	0.30 min		
Carrier pressure	2 psi		
Vial pressure	14 psi		

Results and Discussion

Two examples with different approaches are shown here. The first example uses the concept of statistical residual discrepancies to identify differences between samples.

Fragrance samples were first analyzed using the 4440A, and the results were processed applying the Pirouette chemometrics software. Figure 1 is a PCA plot of four reference standards and replicates of an out-of-spec product separated from the standards. The out-of-spec product can be differentiated easily from the standards without knowing the constituents of the samples. One of the unique features of the 4440A chemical sensor is that it can help identify the unknown chemical(s) that caused samples to be different.

The next step is to use the Pirouette software to run SIMCA (Soft Independent Modeling of Class Analogy) analysis and predict the same samples against the SIMCA model. Because the impurity or differentiating compound is the chemical that caused the samples to cluster away from the standards, the ions (mass fragments) that do not match the profile of the standard samples are likely the cause of the contamination. Therefore, the ions with large x-residuals values (shown in figure 2) are likely to be the differentiating compound. In figure 2, masses 55, 69, 73, 111, and 129 are clearly ions that do not fit the profile of the standard samples.

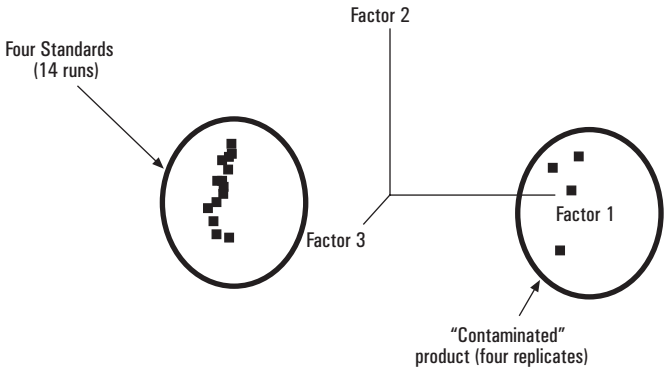

Figure 1. PCA plot of reference standards and contaminated sample.

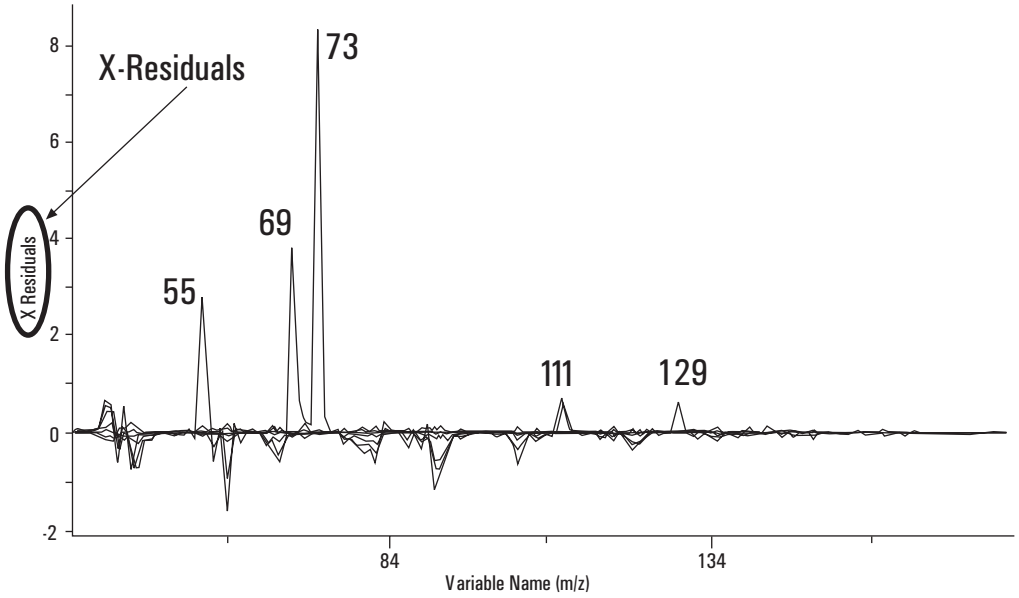

Figure 2. The x-residuals (discrepancies) of the standard samples and the contaminated samples.

The following step is to analyze the out-of-spec product by HS/GC/MS in the scan mode. The result is the TIC shown in figure 3. Plotting the extracted ions with large x-residuals (figure 4) makes it easy to locate the compound that caused the sample to be bad or different. Figure 5 shows the extracted ion chromatograms (EICs) of some of the masses identified in figure 2.

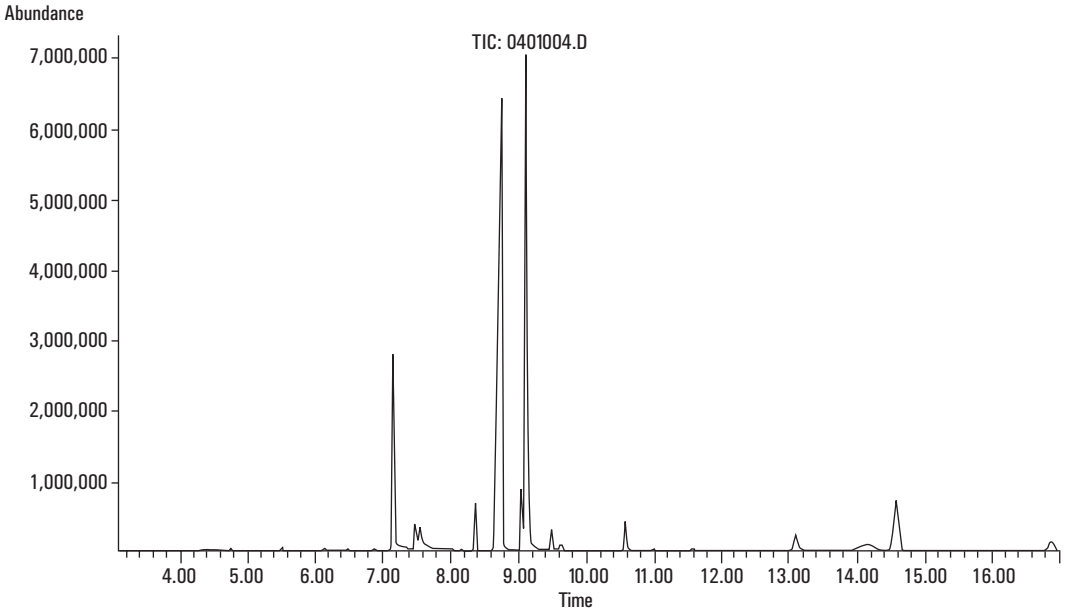

Figure 3. The total ion chromatogram (TIC) of the out-of-spec sample from an HS/GC/MS analysis.

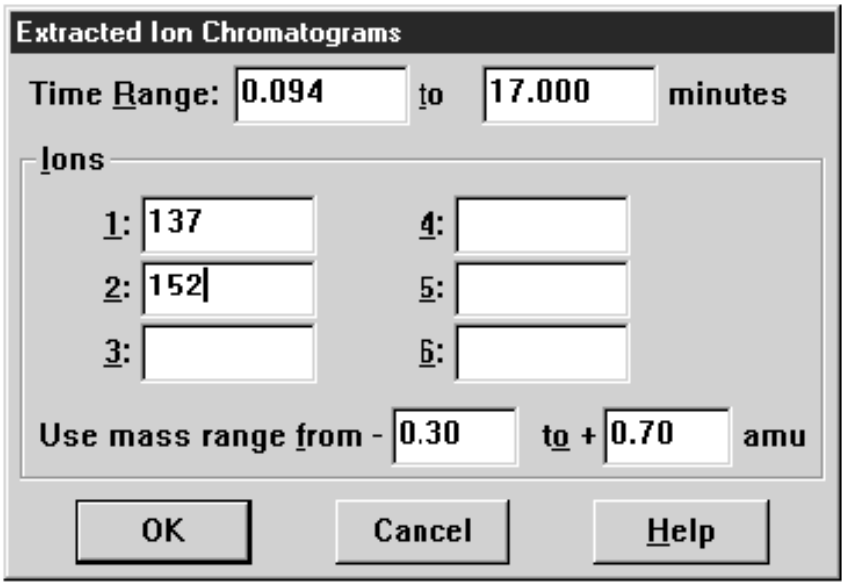

Figure 4. Masses selected for the extracted ion chromatograms, 73, 111, and 129.

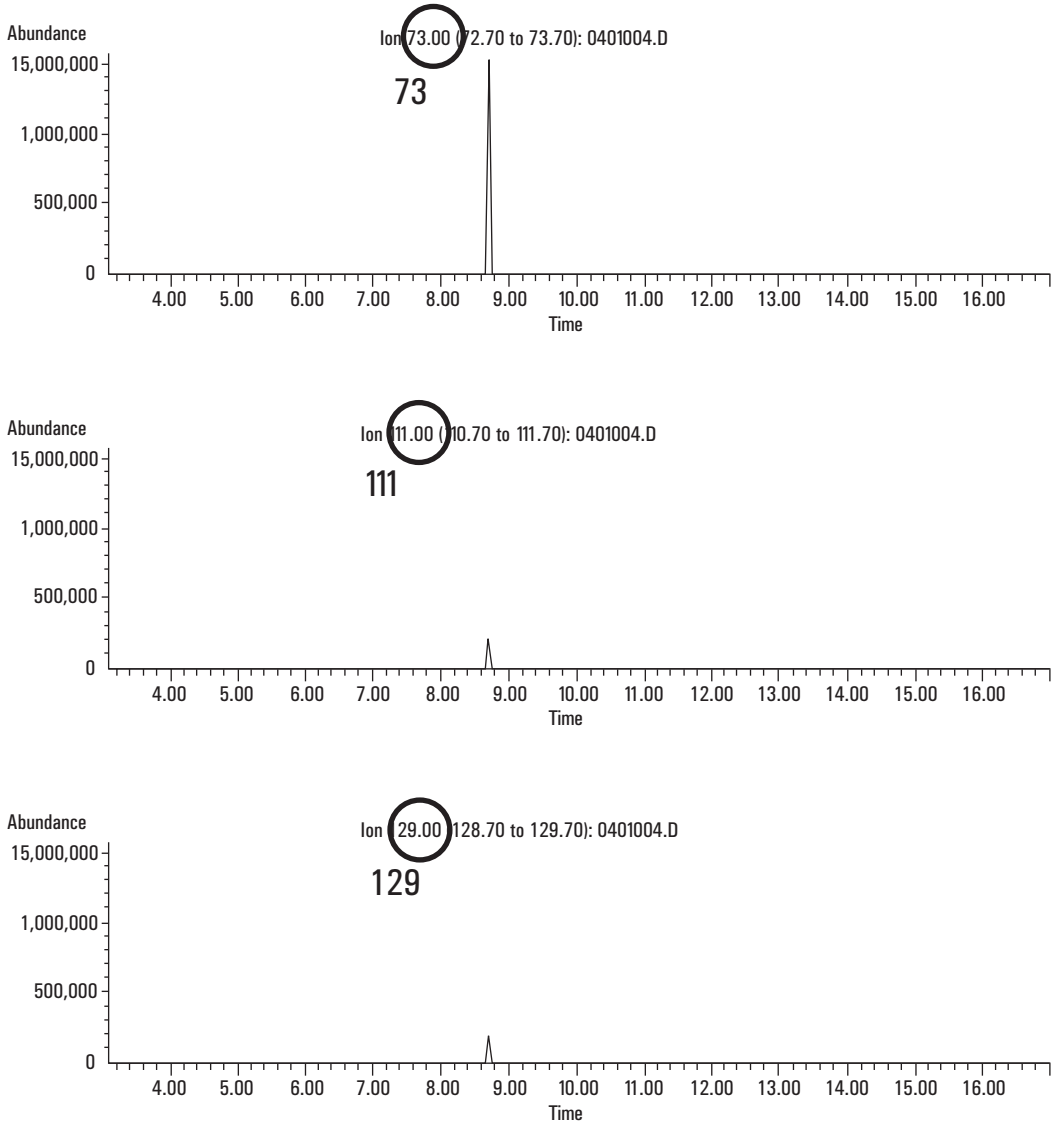

Figure 5. Extracted ion chromatograms of masses 73, 111, and 129 from the results of figure 3.

The last step is to zoom in the area that has peaks and obtain the mass spectrum where the apexes of the EICs are aligned at retention time 8.704 min (illustrated in figure 6). This is the spectrum of the chemical that caused the out-of-spec sample.

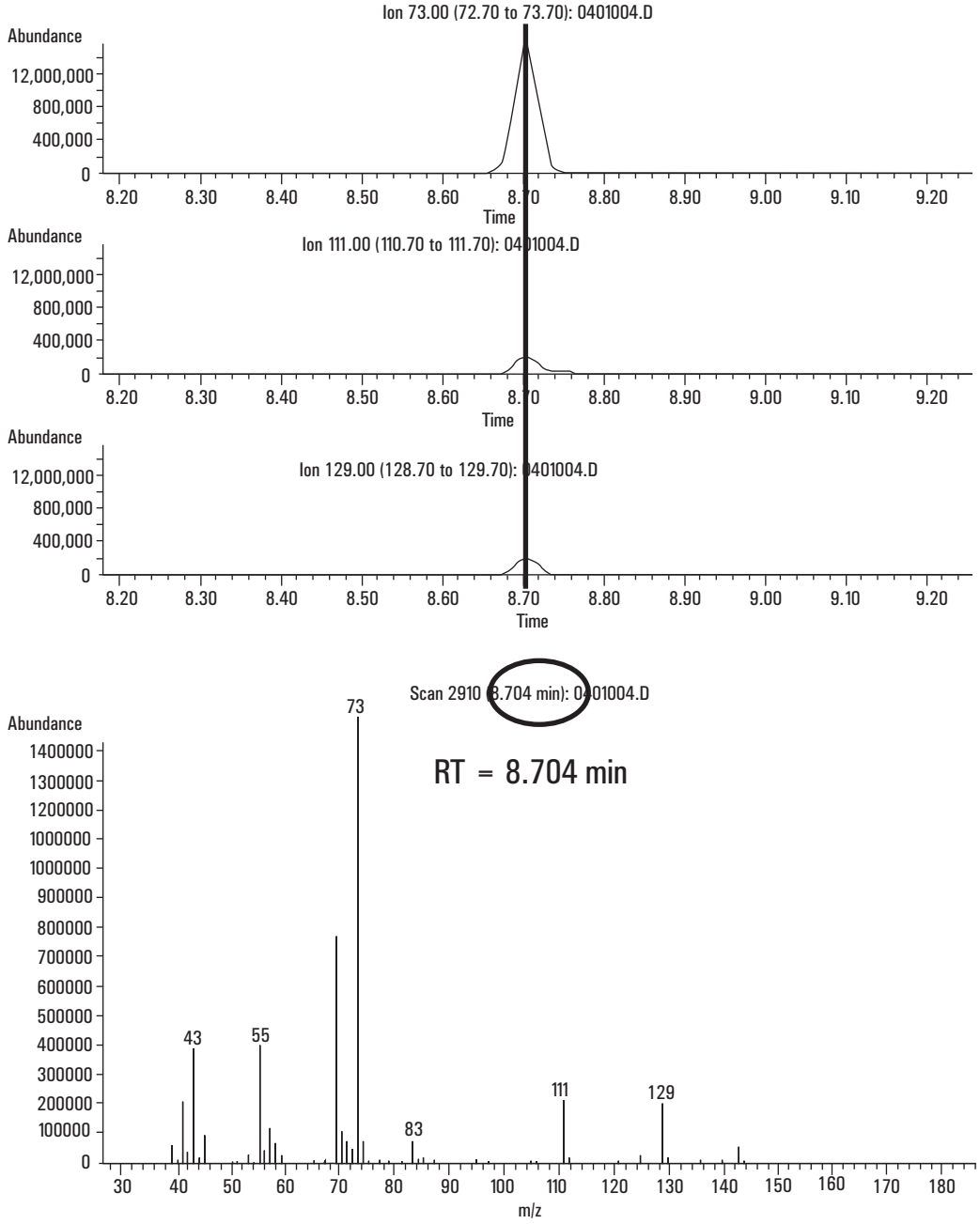

Figure 6. The mass spectrum at the apex of the extracted ion chromatograms.

A simple mass spectral library search enables easy identification of the impurity (figure 7). In this case, the out-of-spec sample contains 2 percent impurity.

The second approach uses the chemometrics discriminating power function to identify the differences between samples.

As with the previous approach, fragrance samples were first analyzed using the 4440A. The results were processed using the Pirouette chemometrics software. Figure 8 presents a PCA plot of four reference standards and replicates of an out-of-spec product separated from the standards. One of the functions in SIMCA is to calculate the discriminating power of

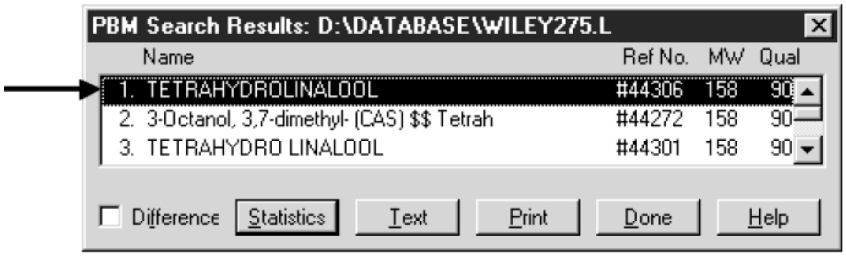

Figure 7. The impurity identified by a mass spectral library search.

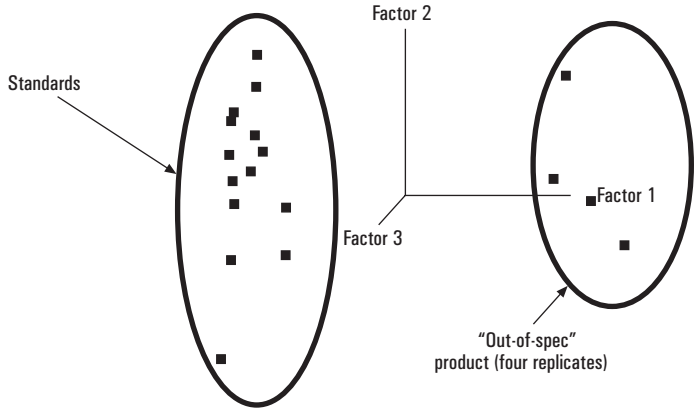

Figure 8. PCA plot of reference standards and out-of-spec sample.

each mass in differentiating two sample groups. The chemometrics software determines which m/z values are most important for differentiating samples. For example, masses (m/z) 137 and 152 shown in figure 9 are the most significant discriminating ions that separated the standards and the out-of-spec product.

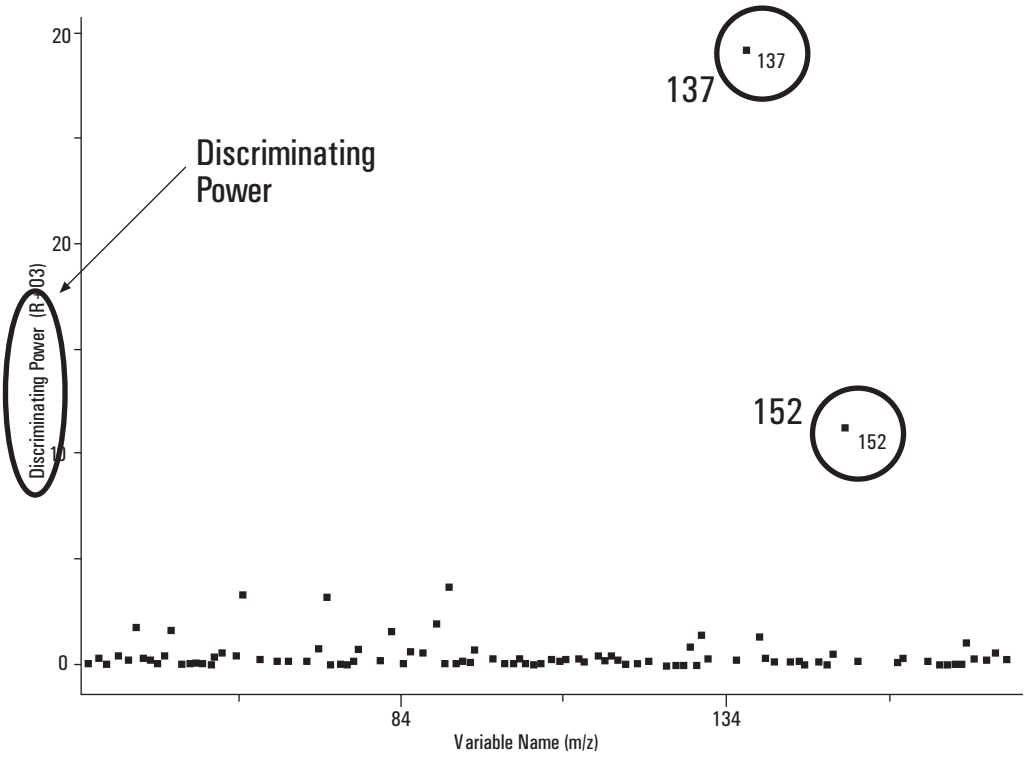

Figure 9. Discriminating power of each mass (m/z) as calculated by the chemometrics data analysis program.

Again, the next step is to analyze the out-of-spec product by HS/GC/MS in the scan mode. The result gives the TIC shown in figure 10. Plotting the extracted ions with high

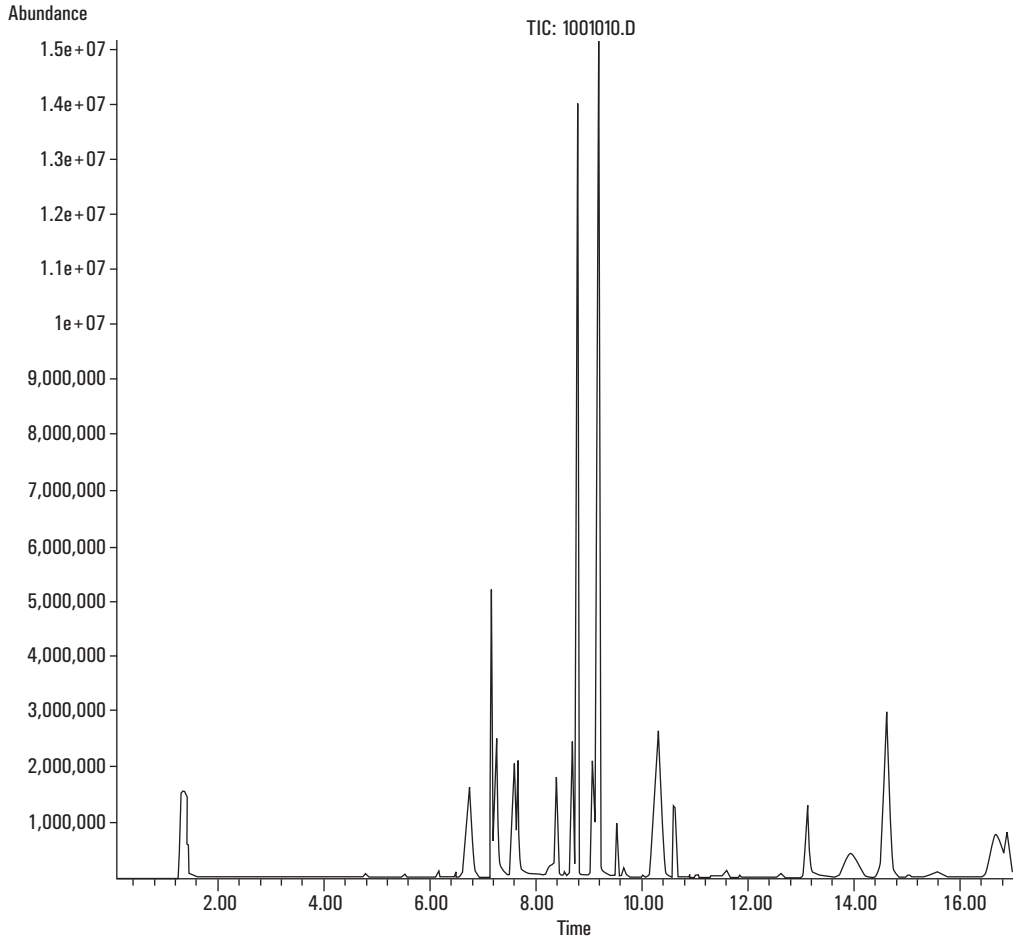

Figure 10. The total ion chromatogram of the out-of-spec sample from an HS/GC/MS analysis.

discriminating power (figure 11) makes it easy to locate the compound that caused the sample to be bad or different. Figure 12 presents the EICs of some of the masses identified in figure 9.

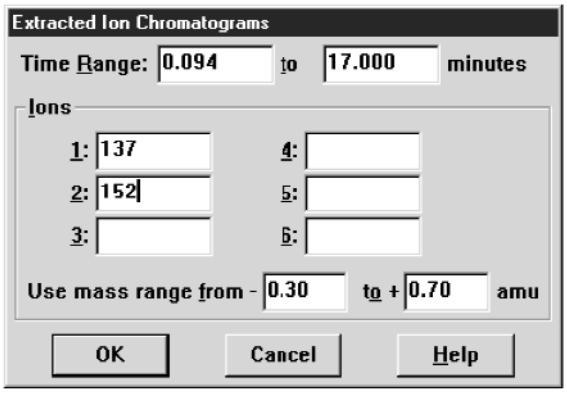

Figure 11. Masses selected for the extracted ion chromatograms, 137 and 152.

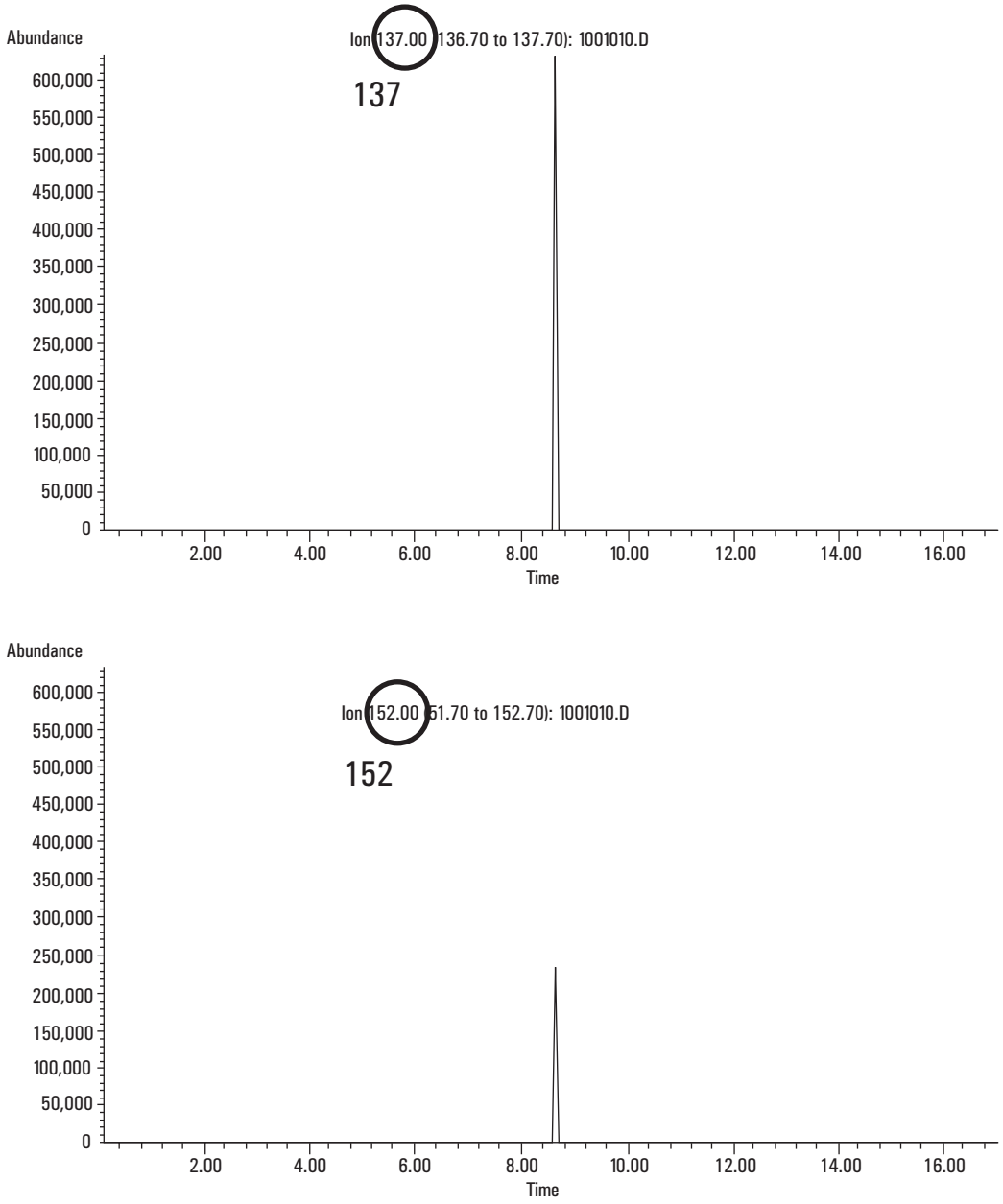

Figure 12. Extracted ion chromatograms of masses 137 and 152 from the results of figure 10.

The final step, again, is to zoom in the area that has peaks and obtain the mass spectrum where the apexes of the EICs are aligned at retention time 8.652 min (figure 13). This is the

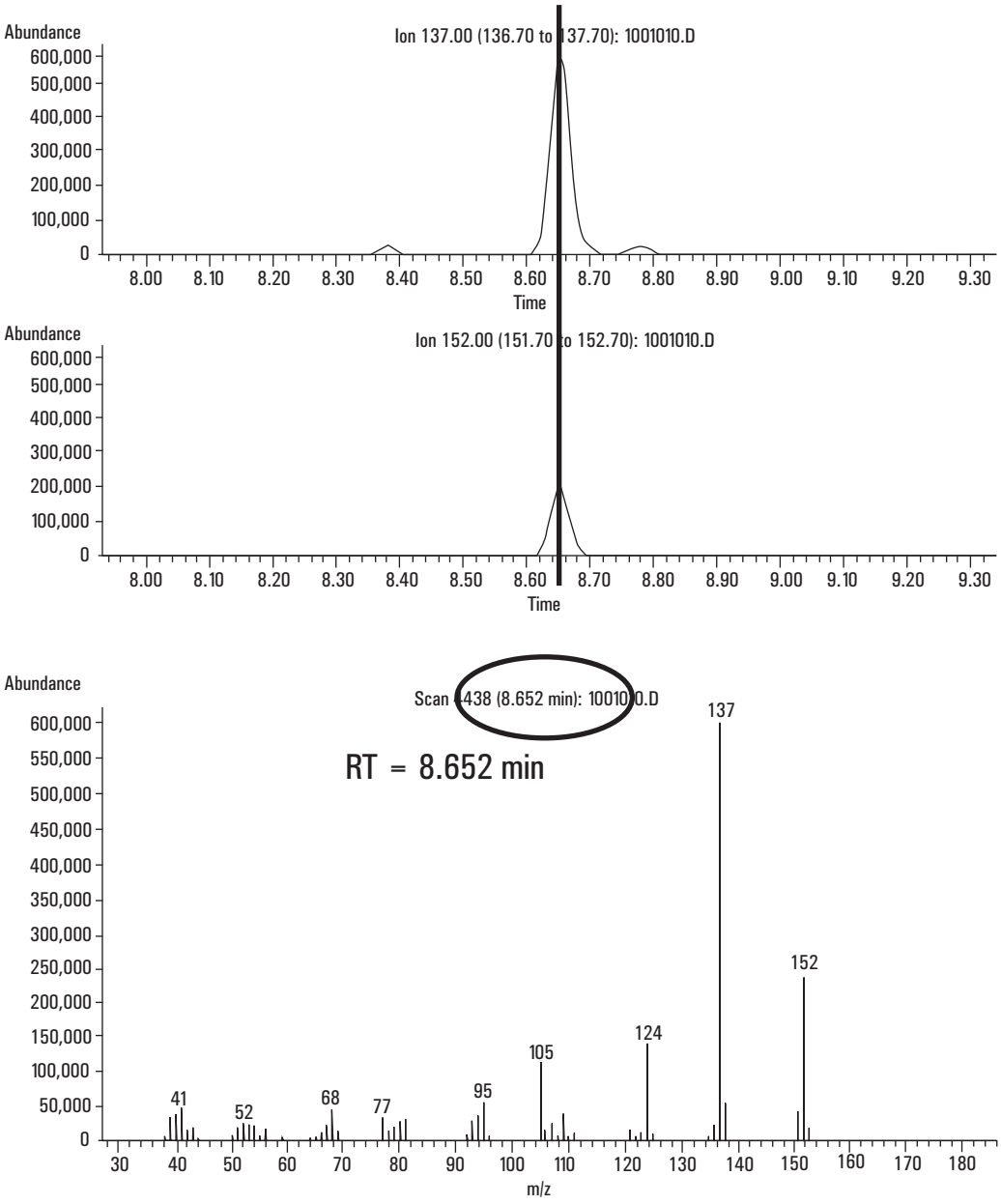

Figure 13. The mass spectrum at the apex of the extracted ion chromatograms.

spectrum of the chemical that caused the sample to be out-of-spec. A simple mass spectral library search enables easy identification of the impurity (figure 14). Figure 15 shows the location of the impurity on the total ion chromatogram. This out-of-spec sample contained 0.15 percent impurity.

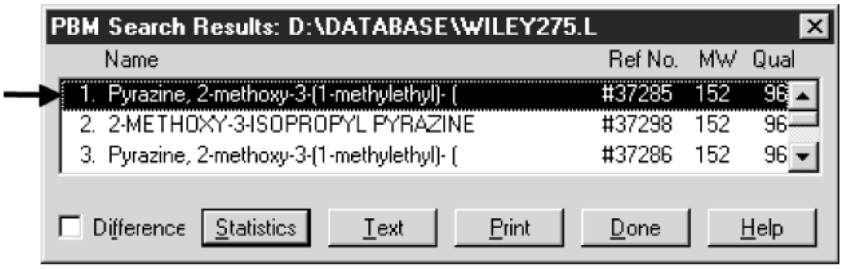

Figure 14. The impurity identified by a mass spectral library search.

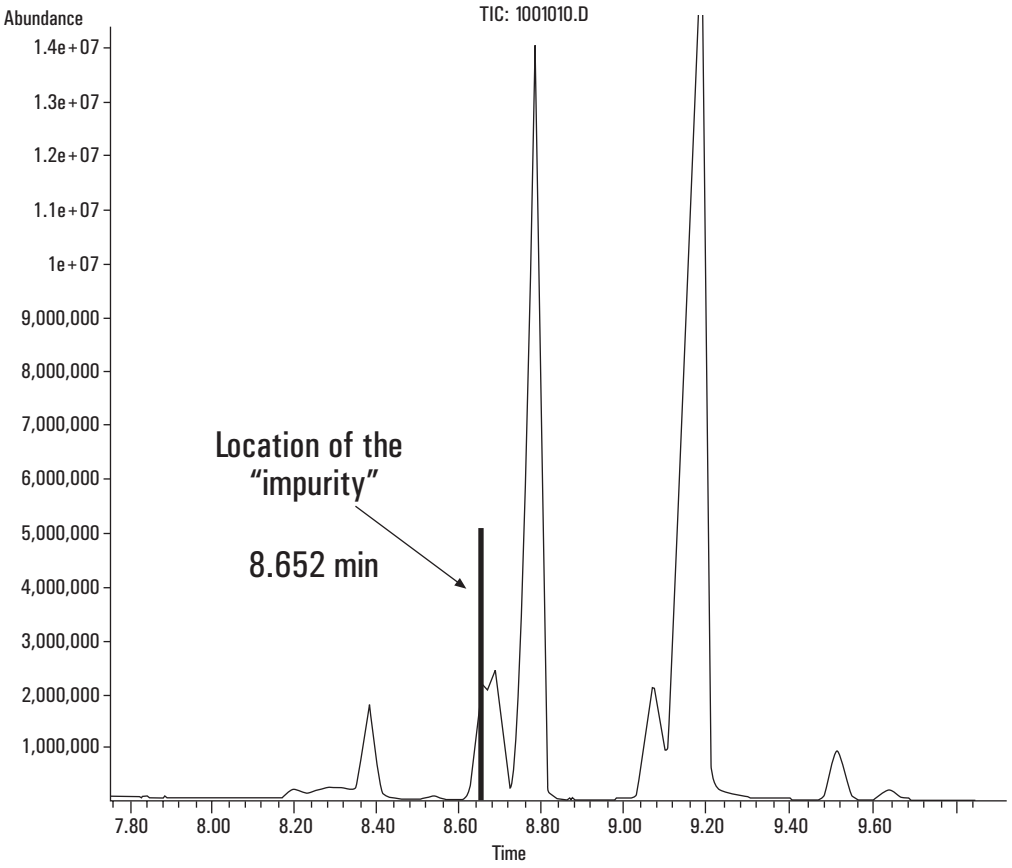

Figure 15. The location of the impurity on the total ion chromatogram.

If the HS/GC/MS system is not readily available, the impurity can be identified sometimes by using the "Parametric Retrieval" tool in the MSD ChemStation software of the chemical sensor. Several possible candidates may be "retrieved" by searching the masses selected by the x-residuals or the discriminating power function. The mass fragment pattern of each candidate may reveal the identity of the impurity, as illustrated in figure 16.

If the analyst does not know where to look for the impurity in the TIC, it is difficult and time-consuming to locate and identify the compound. The 4440A chemical sensor can provide the information (masses) to help the analyst understand why products are different (or out-of-spec). Without positive identification, one can operate the chemical sensor in the selected ion monitoring (SIM) mode to differentiate any out-of-spec product with maximum sensitivity. If compound identification is required, it is easy to apply the information from the 4440A to the HS/GC/MS results to identify the impurity.

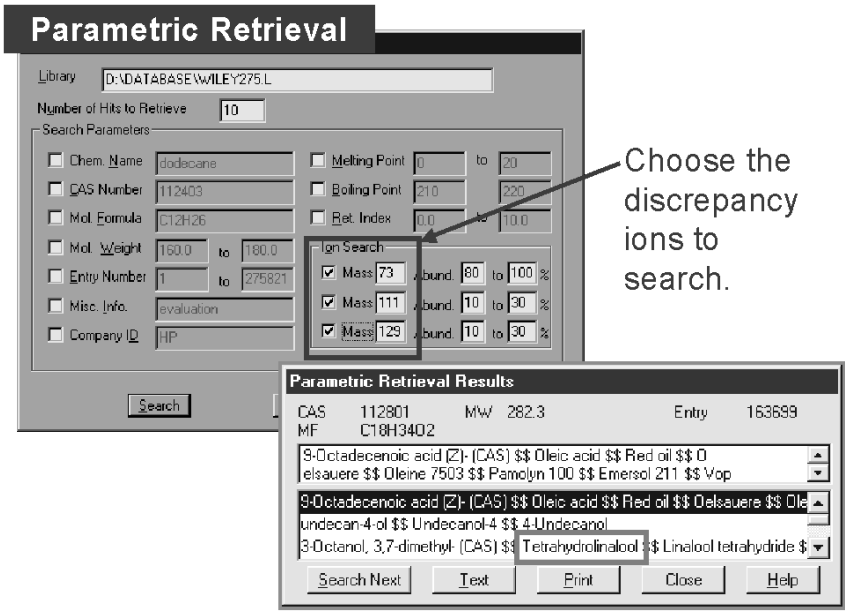

Figure 16. An impurity can be identified sometimes without HS/GC/MS analysis by using the mass fragment pattern (shown in figure 6) and the parametric retrieval tool in the MSD ChemStation software.

Summary

These results show that the Agilent 4440A chemical sensor can help locate and identify contaminated raw materials and out-of-spec final products, quickly and easily, without knowing the constituents of a sample. This is especially useful in the QA/QC area. Furthermore, using masses selected by the x-residuals or the discriminating power function, the Agilent 4440A can also help identify the impurity using an HS/GC/MS system. Therefore, it can be advantageous to use the mass selective sensor in R&D and/or QC to complement an HS/GC/MS system.

Acknowledgment

The authors would like to thank Dr. Neugebauer (DRAGOCO Gerberding & Co. AG) for providing the samples used in this study. DRAGOCO, headquartered in Germany, is one of the leading international suppliers of perfume compositions, aroma chemicals, cosmetic raw materials and active ingredients, and flavors.

Reference

1. C. Kai Meng, Philip L. Wylie, and Cynthia Cai, "Classifying Citrus Products with a Chemical Sensor," *Food Testing & Analysis*, Oct/Nov 1998, pp 17-18.

Printed in the USA 3/2000
5968-3944E

Agilent Technologies
Innovating the HP Way